

AMENDMENTS

IN THE SPECIFICATION:

Please replace Table 2 of the specification with the copy of Table 2 attached to this submission.

Please replace the paragraph spanning pages 23-25 with the following paragraph, provided in clean format in accordance with 37 C.F.R. § 1.121. A marked-up version of the paragraph, showing the changes Applicants have made is in Appendix A.

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Enhancement agents contemplated in this invention include plant growth regulators, particularly auxin-related growth regulators, which will include auxins, compounds with auxin-like activity, and auxin antagonists. Auxin-related growth regulators will typically be incorporated in the medium at concentrations of between 10^{-10} M to 10^{-3} M, preferably between 10^{-8} to 10^{-5} M. Most preferred examples of auxin-related growth regulators include 1-Naphthaleneacetic acid, 2-Naphthaleneacetic acid, 1-Naphthaleneacetamide / Naphthylacetamide, N-(1-Naphthyl)phthalamic acid, , 1-Naphthoxyacetic acid, 2-Naphthoxyacetic acid, beta-Naphthoxyacetic acid, 1-Naphthoxyacetamide,, 3-Chlorophenoxyacetic acid, 4-Chlorophenoxyacetic acid, 4-Iodophenoxyacetic acid, Indoleacetamide, Indoleacetic acid , Indoyleacetate, Indoleacetyl leucine, Gamma-(3-Indole)butyric acid, 4-Amino-3,5,6-trichloropicolinic acid, 4-Amino-3,5,6-trichloropicolinic acid methyl ester, 3,6-Dichloro-o-anisic acid, 3,7-Dichloro-8-quinolinecarboxylic acid, Phenylacetic acid, 2-Iodophenylacetic acid, 3-Iodophenylacetic acid, 2-Methoxyphenylacetic acid, Chlorpropham, 4-chloroindole-3-acetic acid, 5-Chloroindole-3-acetic acid, 5-Bromo-4-chloro-3-indoyl butyrate, Indoleacetyl phenylalanine, Indoleacetyl glycine, Indoleacetyl alanine, 4-chloroindole, p-chlorophenoxyisobutyric acid, 1-pyrenoxylbenzoic acid, Lysophosphatidic acid, 1-naphthyl-N-methylcarbamate, and Ethyl-5-chloro-1H-Indazole-3-ylacetate-3-Indolebutanoic acid. Other preferred examples of auxin-related growth regulators include Naphthalene-2,6-dicarboxylic acid, Naphthalene-1,4,5,8-tetracarboxylic acid dianhydride, Naphthalene-2-sulfonamide, 4-Amino-3,6-disulfo-1,8-naphthalic anhydride, 3,5-

dimethylphenoxyacetic acid, 1,8-Naphthalimide, 2,4-Dichlorophenoxyacetic acid, 2,3-Dichlorophenoxyacetic acid, 2,3,5-Trichlorophenoxyacetic acid, 2-Methyl-4-chlorophenoxyacetic acid, Nitrophenoxyacetic acids, DL-alpha-(2,4-Dichlorophenoxy)propionic acid, D-alpha-(2,4-Dichlorophenoxy)propionic acid, 4-Bromophenoxyacetic acid, 4-Fluorophenoxyacetic acid, 2-Hydroxyphenoxyacetic acid, 5-Chloroindole, 6-Chloro-3-indoylacetate, 5-Fluoroindole, 5-Chloroindole-2-carboxylic acid, 3-Chloroindole-2-carboxylic acid, Indole-3-pyruvic acid, 5-Bromo-4-chloro-3-indoylbutyrate, 6-Chloro-3-indoylbutyrate, Quinoline-2-thioglycolic acid, Aminophenylacetic acids, 3-Nitrophenylacetic acid, 3-Chloro-4-hydroxybenzoic acid, Chlorflurenol, 6-Chloro-3-indoyl acetate, N-(6-aminohexyl)-5-chloro-1-Naphthalenesulfonamide hydrochloride, 2-chloro-3(2,3-dichloro-phenyl) propionitrile, o-chlorophenoxyacetic acid, 6,7-dimethoxy-1,2-benzisoxazole-3-acetic acid, 3-oxo-1,2-benzisothiazoline-2-ylacetic acid, Mastoparan, 2,3,5-Triidobenzoic acid, 2-(3-chlorophenoxy)propanoic acid, and Mecoprop. Other examples of suitable auxin-related growth regulators include Naphthoic acid hydrazide, 2,4-Dibromophenoxyacetic acid, 3-Trifluoromethylphenoxyacetic acid, Oxindole, Indole-2-carboxylic acid, Indole-3-lactic acid, Beta-(3-Indole)propionic acid, 2-Bromophenylacetic acid, 3-Bromophenylacetic acid, 2-Chlorophenylacetic acid, 3-Chlorophenylacetic acid, 2-Methylphenylacetic acid, 3-Methylphenylacetic acid, 3-Trifluoromethylphenylacetic acid, 3-Methylthiophenylacetic acid, Phenylpropionic acid, 4-chloro-2-methylphenylthioacetic acid, 2-Chlorobenzoic acid, 3-Chlorobenzoic acid, 2,3-Dichlorobenzoic acid, 3,4-Dichlorobenzoic acid, 2,3,5-Trichlorobenzoic acid, 2,4,6-Trichlorobenzoic acid, 2-Benzothiazoleoxyacetic acid, 2-Chloro-3-(2,3-dichlorophenyl)propionitrile, 2,4-Diamino-s-triazine, Naphthalic anhydride, Dikegulac, chlorflurecolmethyl ester, 2-(p-chlorophenoxy)-2-methylpropionic acid, 2-chloro-9-hydroxyfluorene-9-carboxylic acid, 2,4,6-trichlorophenoxyacetic acid, 2-(p-chlorophenoxy)-2-methylpropionic acid, Ethyl 4-(chloro-o-tolyloxy)butyrate, [N-(1,3-dimethyl-1H-Pyrazol-5-yl)-2-(3,5,6-Trichloro-2-pyridinyl)oxy]acetamide, 4-Chloro-2-oxobenzothiazolin-3-yl-acetic acid, 2-(2,4-Dichlorophenoxy)propanoic acid, 2-

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(2,4,5-Trichlorophenoxy) propanoic acid, 4-Fluorophenylacetic acid, 3-Hydroxyphenylacetic acid, Orthonil, 3,4,5-Trimethoxycinnamic acid, 2(3,4-dichlorophenoxy)triethylamine, Indole-3-propionic acid, Sodium Ioxynil, 2-Benzothiazoleacetic acid, and (3-phenyl-1,2,4-thiadiazol-5-yl)thioacetic acid.

IN THE CLAIMS

Please replace claims 1, 24-27, 29, 32, 34, 43, 45-48, 50, 68-69, 71 and 72 with the following claims, provided in a clean format in accordance with 37 C.F.R. § 1.121. A marked-up version of the claims, showing the changes Applicants have made are in Appendix A.

E2
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1. (twice amended) A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein at least one of the one or more nutrient media comprises one or more enhancement agents selected from the group consisting of (a) jasmonate-related compounds or alkyl esters thereof, (b) antiethylene agents, and (c) inhibitors of phenylpropanoid metabolism.

24. (amended) The method of claim 18, wherein the concentration of silver ions, silver complexes, or silver-containing compounds is 10 μ M – 100 μ M

E2

25. (amended) The method of claim 18, wherein the concentration of silver ions, silver complexes, or silver-containing compounds is 50 μ M.

26. (amended) The method of claim 18, wherein the concentration of silver ions, silver complexes, or silver-containing compounds is 10 μ M.

E3

27. The method of claim 18, wherein silver and jasmonate are present in the one or more nutrient media in molar ratio of silver:jasmonate of less than 9.5.

E4

29. The method of claim 28, wherein the inhibitor of phenylpropanoid metabolism is selected from the group consisting of 3,4-methylenedioxynitrocinnamic acid, 3,4-methylenedioxycinnamic acid, 3,4-methylenedioxy-phenylpropionic acid, 3,4-methylenedioxyphenylacetic acid, 3,4-methylenedioxybenzoic acid, 3,4-trans-

E4
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dimethoxycinnamic acid, 4-hydroxycinnamic acid, phenylpropionic acid, fluorophenylalanine, 1-aminobenzotriazole, 2-hydroxy-4,6-dimethoxybenzoic acid, 2-(diethylamino)ethyl ester of α -phenyl- α -propylbenzeneacetic acid, ammonium oxalate, vinylimidazole, diethyldithiocarbamic acid, and sinapic acid. ?

32. The method of claim 1 or claim 30, wherein the one or more nutrient media further comprise an auxin-related growth regulator selected from the group consisting of 1-Naphthaleneacetic acid, 2-Naphthaleneacetic acid, 1-Naphthaleneacetamide/Naphthylacetamide, N-(1-Naphthyl)phthalamic acid, , 1-Naphthoxyacetic acid, 2-Naphthoxyacetic acid, beta-Naphthoxyacetic acid, 1-Naphthoxyacetamide,, 3-Chlorophenoxyacetic acid, 4-Chlorophenoxyacetic acid, 4-Iodophenoxyacetic acid, Indoleacetamide, Indoleacetic acid , Indoylacetate, Indoleacetyl leucine, Gamma-(3-Indole)butyric acid, 4-Amino-3,5,6-trichloropicolinic acid, 4-Amino-3,5,6-trichloropicolinic acid methyl ester, 3,6-Dichloro-o-anisic acid, 3,7-Dichloro-8-quinolinecarboxylic acid, Phenylacetic acid, 2-Iodophenylacetic acid, 3-Iodophenylacetic acid, 2-Methoxyphenylacetic acid, Chlorpropham, 4-chloroindole-3-acetic acid, 5-Chloroindole-3-acetic acid, 5-Bromo-4-chloro-3-indoyl butyrate, Indoleacetyl phenylalanine, Indoleacetyl glycine, Indoleacetyl alanine, 4-chloroindole, p-chlorophenoxyisobutyric acid, 1-pyrenoxylbenzoic acid, Lysophosphatidic acid, 1-naphthyl-N-methylcarbamate, Ethyl-5-chloro-1H-Indazole-3-ylacetate-3-Indolebutanoic acid, Naphthalene-2,6-dicarboxylic acid, Naphthalene-1,4,5,8-tetracarboxylic acid dianhydride, Naphthalene-2-sulfonamide, 4-Amino-3,6-disulfo-1,8-naphthalic anhydride, 3,5-dimethylphenoxyacetic acid, 1,8-Naphthalimide, 2,4-Dichlorophenoxyacetic acid, 2,3-Dichlorophenoxyacetic acid, 2,3,5-Trichlorophenoxyacetic acid, 2-Methyl-4-chlorophenoxyacetic acid, Nitrophenoxyacetic acids, DL-alpha-(2,4-Dichlorophenoxy)propionic acid, D-alpha-(2,4-Dichlorophenoxy)propionic acid, 4-Bromophenoxyacetic acid, 4-Fluorophenoxyacetic acid, 2-Hydroxyphenoxyacetic acid, 5-Chloroindole, 6-Chloro-3-indoylacetate, 5-Fluoroindole, 5-Chloroindole-2-carboxylic acid, 3-Chloroindole-2-carboxylic acid, Indole-3-pyruvic acid, 5-Bromo-4-chloro-3-indoylbutyrate, 6-Chloro-3-indoylbutyrate, Quinoline-2-thioglycolic acid, Aminophenylacetic acids, 3-Nitrophenylacetic acid, 3-Chloro-4-hydroxybenzoic acid, Chlorfurenol, 6-Chloro-3-indoyl acetate, N-(6-aminoethyl)-5-chloro-1-Naphthalenesulfonamide hydrochloride, 2-chloro-3(2,3-dichloro-phenyl) propionitrile, o-

E5

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chlorophenoxyacetic acid, 6,7-dimethoxy-1,2-benzisoxazole-3-acetic acid, 3-oxo-1,2-benzisothiazoline-2-ylacetic acid, (Mastoparan), 2,3,5-Triidobenzoic acid, 2-(3-chlorophenoxy)propanoic acid, (Mecoprop), Naphthoic acid hydrazide, 2,4-Dibromophenoxyacetic acid, 3-Trifluoromethylphenoxyacetic acid, (Oxindole), Indole-2-carboxylic acid, Indole-3-lactic acid, Beta-(3-Indole)propionic acid, 2-Bromophenylacetic acid, 3-Bromophenylacetic acid, 2-Chlorophenylacetic acid, 3-Chlorophenylacetic acid, 2-Methylphenylacetic acid, 3-Methylphenylacetic acid, 3-Trifluoromethylphenylacetic acid, 3-Methylthiophenylacetic acid, Phenylpropionic acid, 4-chloro-2-methylphenylthioacetic acid, 2-Chlorobenzoic acid, 3-Chlorobenzoic acid, 2,3-Dichlorobenzoic acid, 3,4-Dichlorobenzoic acid, 2,3,5-Trichlorobenzoic acid, 2,4,6-Trichlorobenzoic acid, 2-Benzothiazoleoxyacetic acid, 2-Chloro-3-(2,3-dichlorophenyl)propionitrile, 2,4-Diamino-s-triazine, Naphthalic anhydride, Dikegulac, chlorflurecolmethyl ester, 2-(p-chlorophenoxy)-2-methylpropionic acid, 2-chloro-9-hydroxyfluorene-9-carboxylic acid, 2,4,6-trichlorophenoxyacetic acid, 2-(p-chlorophenoxy)-2-methyl propionic acid, Ethyl 4-(chloro-o-tolyloxy)butyrate, [N-(1,3-dimethyl-1H-Pyrazol-5-yl)-2-(3,5,6-Trichloro-2-pyridinyl)oxy]acetamide, 4-Chloro-2-oxobenzothiazolin-3-yl-acetic acid, 2-(2,4-Dichlorophenoxy)propanoic acid, 2-(2,4,5-Trichlorophenoxy) propanoic acid, 4-Fluorophenylacetic acid, 3-Hydroxyphenylacetic acid, Orthonil, 3,4,5-Trimethoxycinnamic acid, 2(3,4-dichlorophenoxy)triethylamine, Indole-3-propionic acid, Sodium Ioxynil, 2-Benzothiazoleacetic acid, and (3-phenyl-1,2,4-thiadiazol-5-yl)thioacetic acid.

E6

34. The method of claim 30, wherein the inhibitor of phenylpropanoid metabolism is selected from the group consisting of 3,4,-methylenedioxy-nitrocinnamic acid, 3,4,-methylenedioxy-cinnamic acid, 3,4,-methylenedioxy-phenylpropionic acid, 3,4,-methylenedioxyphenylacetic acid, 3,4,-methylenedioxybenzoic acid, 3,4,-trans-dimethoxycinnamic acid, 4-hydroxycinnamic acid, phenylpropionic acid, fluorophenylalanine, 1-aminobenzotriazole, 2-hydroxy-4,6-dimethoxybenzoic acid, 2-(diethylamino)ethyl ester of α -phenyl- α -propylbenzeneacetic acid, ammonium oxalate, vinylimidazole, diethyldithiocarbamic acid, and sinapic acid.

E7

43. (amended) The method of claim 42, wherein the concentration of nitrate is lower in the second medium than in the first medium, and the concentration of a saccharide is higher in the second medium than in the first medium.

E8 45. (amended) The method of claim 42, wherein the second medium contains a saccharide at a concentration which is 2 to 5 times the saccharide concentration in the first medium.

E9 46. (thrice amended) The method of claim 1, wherein the cells are cultured in media containing a saccharide in a concentration of 1 – 150 g/L, nitrate ion in a concentration of 0.3 – 70 mM or a combination thereof.

E10 47. (amended) The method of claim 43, wherein the first medium contains a saccharide in the concentration of 1 – 30 g/L, and nitrate ion in the concentration of 2.5 – 70 mM; and the second medium contains a saccharide in the concentration of 4 – 150 g/L, and nitrate ion in the concentration of 0.3 – 18 mM.

E11 48. (amended) The method of claim 43, wherein the first medium contains a saccharide in the concentration of 5 – 15 g/L, and nitrate ion in the concentration of 20 – 30 mM; and the second medium contains a saccharide in the concentration of 35 – 55 g/L, and nitrate ion in the concentration of 2 – 7 mM.

E12 50. The method of claim 1 or claim 30, wherein said the medium which induces taxane production is replenished during cultivation by periodically replenishing nutrient medium components and removing spent medium.

E13 68. A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein at least one of the one or more nutrient media comprises a compound selected from the group consisting of polyamines.

E14 69. (amended) The method of claim 68, wherein said polyamines are added to at least one of the one or more nutrient media. ?

E15 71. The method of claim 2, wherein the concentration of silver ions, silver complexes, or silver-containing compounds is 0.01 μ M – 10 μ M.

E14
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72. A method for producing one or more taxanes in high yields in cell culture of a *Taxus* species comprising: cultivating in suspension culture, in one or more nutrient media under growth and product formation conditions, cells of a *Taxus* species derived from callus or suspension cultures, and recovering said one or more taxanes from said cells, said medium of said cell culture, or both, wherein β -phenylalanine is added to the one or more nutrient media in an amount sufficient to enhance taxane production.

how much,